

What is claimed is:

1 1. An array comprising a support having at least
2 three discrete regions, a first region bearing a pool of
3 polynucleotide probes comprising first and second probes, a
4 second region bearing the first probe without the second probe
5 and a third region bearing the second probe without the first
6 probe.

1 2. The array of claim 1, wherein the first and
2 second probes are respectively complementary to first and
3 second nonoverlapping segments of a target sequence.

1 3. The array of claim 2, wherein
2 the first and second nonoverlapping segments of the
3 target nucleic acid respectively contain first and second
4 polymorphic sites, and
5 the first probe is complementary to a polymorphic
6 form of the first site and the second probe is complementary
7 to a polymorphic form of the second site.

1 4. The array of claim 3, wherein the second region
2 bears the first probe with a third probe as a second pool of
3 polynucleotide probes, and the third region bears the second
4 probe with a fourth probe, as a third pool of polynucleotide
5 probes.

1 5. The array of claim 4, wherein the third probe is
2 complementary to a second polymorphic form of the second
3 polymorphic site, and the fourth probe is complementary to a
4 second polymorphic form of the first polymorphic site.

1 6. An array comprising a substrate having a
2 plurality of discrete regions, different regions bearing
3 different pools of probes, a pool of probes comprising first
4 and second probes complementary to nonoverlapping segments of
5 a target sequence.

7. The array of claim 6, wherein the nonoverlapping segments of the target sequence include first and second polymorphic sites and the first and second probes are respectively complementary to polymorphic forms of the first and second polymorphic sites, the different pools comprising probes complementary to different combinations of polymorphic forms, the different pools differing in the combination of polymorphic forms.

8. The array of claim 6, wherein the first probe is the same in at least a subset of the plurality of pools and the second probe varies in different pools in the subset.

9. The array of claim 6, wherein the pool of probes comprises first and second subsets of probes,
each pool in the first subset of pools having a common first probe and a different second probe,
each pool in the second subset of pools having a common first probe and a different second probe,
the common first probe differing between the first subset of pools and the second subset of pools.

10. An array comprising a support having at least three discrete regions, a first region bearing a pool of polynucleotide probes comprising first and second probes at a first molar ratio of first to second probes, a second region bearing the first probe without the second probe or with the second probe present at a second molar ratio of first probe to second probe greater than first molar ratio, and a third region bearing the second probe without the first probe or with the first probe present at a third molar ratio of first probe to second probe less than the first molar ratio.

11. A method of determining linkage of polymorphic forms in a target nucleic acid, comprising:
hybridizing a diploid target nucleic acid having first and second polymorphic sites to an array comprising a support having at least three discrete regions, a first region

6 bearing a pool of polynucleotide probes comprising a first
 7 probe complementary to a polymorphic form of the first
 8 polymorphic site and a second probe complementary to a
 9 polymorphic form of the second polymorphic site, a second
 10 region bearing the first probe without the second probe and a
 11 third region bearing the second probe without the first probe;
 12 determining a ratio of binding of the target nucleic
 13 acid to the first region and to the second and third regions
 14 combined to indicate whether the polymorphic form of the first
 15 polymorphic site and the polymorphic form of the second
 16 polymorphic site are present in the same molecule of the
 17 diploid target nucleic acid.

1 12. A method of determining linkage of polymorphic
 2 forms in a target nucleic acid comprising:
 3 hybridizing a diploid target nucleic acid having
 4 first and second polymorphic sites to an array comprising a
 5 support having a plurality of discrete regions, the different
 6 regions bearing different pools of probes, a pool of probe
 7 comprising first and second probes respectively complementary
 8 to polymorphic forms of the first and second polymorphic
 9 sites, the different pools comprising probes complementary to
 10 different combinations of polymorphic forms;
 11 determining binding of the target nucleic acid to
 12 the discrete regions to identify at least one discrete region
 13 that binds more target nucleic acid than an average of target
 14 nucleic acid bound by the discrete regions, the at least one
 15 discrete region bearing a pool of probes respectively
 16 complementary to a combination of polymorphic forms present in
 17 a single molecule of the diploid target nucleic acid.

1 13. The method of claim 12, further comprising
 2 hybridizing a control mixture of a first nucleic acid having a
 3 polymorphic form at the first polymorphic site and a second
 4 nucleic acid having a polymorphic form at the second
 5 polymorphic site and determining hybridization of the mixture
 6 to the discrete regions; determining binding of the control
 7 region to the discrete regions; and comparing binding of the

target nucleic acid and control to the discrete regions to identify a discrete region binding more strongly to the target nucleic acid than the control, this discrete region bearing a pool of probes respectively complementary to a combination of polymorphic forms present in a single molecule of the diploid target nucleic acid.

14. A method of sequencing a target nucleic acid, comprising:

- hybridizing the target nucleic acid to an array comprising a substrate having a plurality of discrete regions bearing different pools of probes, each pool having a common first probe and a different second probe, the common first probe complementary to a known marker in the target,
- determining a sequence of a segment of the target nucleic acid from the relative binding of the target nucleic acid to the pools of probes; and
- mapping the position of the segment in the target sequence relative to the known marker.

15. A method of sequencing a target nucleic acid, comprising

- hybridizing the target nucleic acid to an array comprising a substrate having a plurality of discrete regions, different regions bearing different pools of probes, wherein the pools are subdivided into first and second subarray of pools, each pool in the first subarray of pools having a common first probe and a different second probe, each pool in the second subarray of pools having a common first probe complementary to a known marker in the target, and a different second probe, the common first probe in the first subarray of pools being complementary to a different known marker than in the second subarray of pools;
- determining a sequence of first and second segment of target nucleic acid from the binding of the target nucleic acid to the pools in the first and second subarrays; and

17 mapping the position of first and second segments in
18 the target nucleic acid relative to the positions of the known
19 markers.

1 16. A method of monitoring expression of an mRNA
2 population, comprising:
3 providing a sample comprising a population of mRNA
4 molecules;
5 hybridizing the population of mRNA or nucleic acids
6 copied therefrom to an array comprising a support having a
7 plurality of discrete regions, the different regions bearing
8 different pools of probes, a pool of probe comprising first
9 and second probes respectively complementary to nonoverlapping
10 segments of a known mRNA molecule, the different pools
11 comprising first and second probes complementary to
12 nonoverlapping segments from different known mRNA molecules;
13 determining which discrete regions show specific
14 binding to the population thereby indicating which of the
15 known mRNA molecules are present in the sample.

1 17. The method of claim 16, wherein the support
2 further comprises a second plurality of discrete regions, the
3 different regions bearing different pools of probes, each pool
4 having the same first and second probes except for a single
5 base mismatch in the first or second probe or both as a
6 corresponding pool from the plurality of discrete regions, and
7 the method further comprises comparing binding of
8 corresponding pools of probes from the plurality and second
9 plurality of discrete regions, a difference in binding
10 indicating that the known mRNA to which probes in the pool
11 from the plurality of discrete regions are complementary is
12 present in the sample.

1 18. A method of analyzing a target nucleic acid,
2 comprising:
3 hybridizing a target nucleic acid to an array
4 comprising a support having at least three discrete regions, a
5 first region bearing a pool of polynucleotide probes

E. C. Yeh, *Ph.D., M.S., B.S.*